

Title: Time-to-seizure modeling of lacosamide used in monotherapy in patients with newly diagnosed epilepsy.

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Online resource 3: Supplementary figures

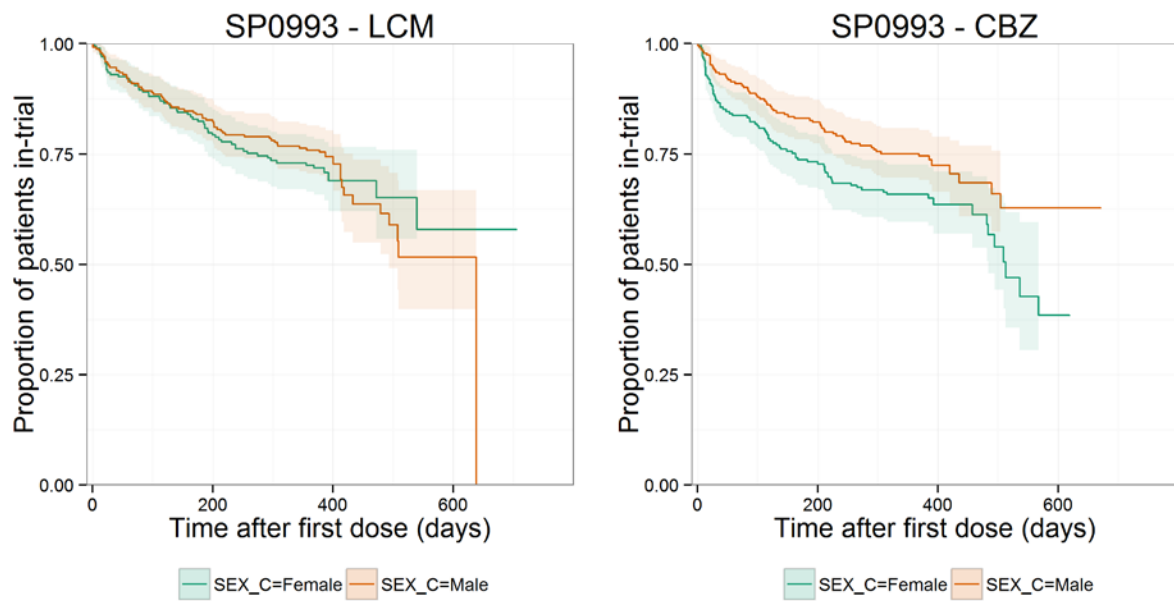


Figure 1: Kaplan-Meier dropout not due to lack of efficacy by SEX. LCM: Lacosamide, CBZ: Carbamazepine.

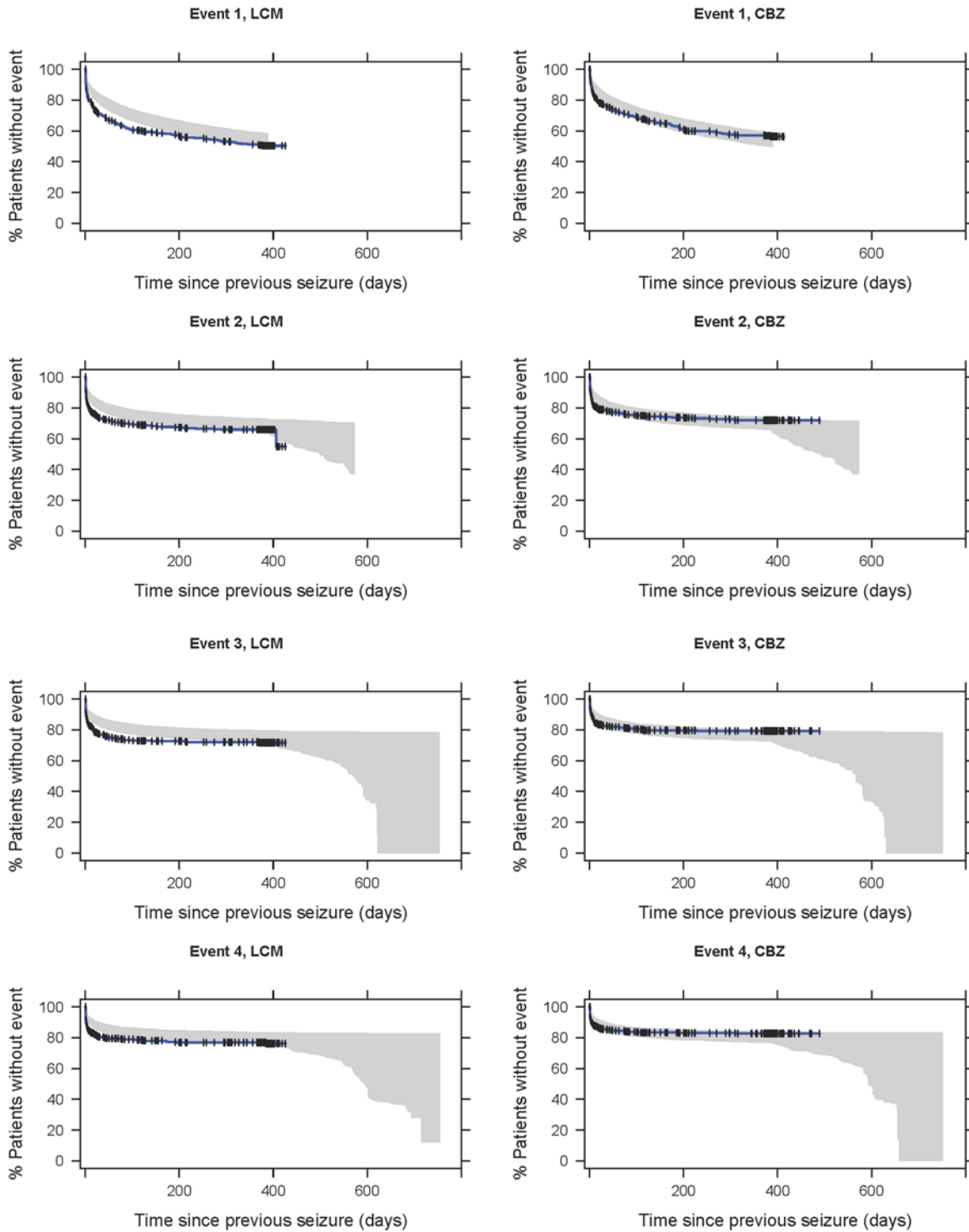


Figure 2: Visual predictive checks of seizure probability split by drug (LCM: lacosamide, CBZ: carbamazepine controlled release). Blue line: observed Kaplan-Meier curve of time to 1st, 2nd, 3rd or 4th event (seizure) after the first dose; shaded area represents the 95% PI based on 500 simulations. Vertical ticks indicate dropouts in the observed data.

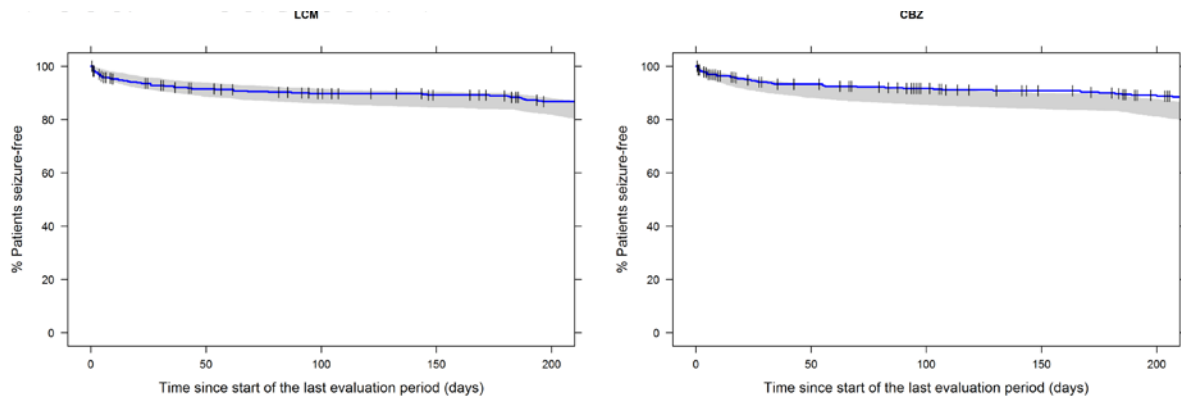


Figure 3: Visual predictive checks of time to first seizure in the evaluation period at the last evaluated dose level. For this outcome parameter, only the first event that happened during the evaluation period of the last dose step of a patient is taken into account. For example, if a patient's dose was escalated to level 3, events from the previous dose steps were not taken into consideration. Blue line: observed Kaplan-Meier curve; shaded area represents the 95% PI based on 500 simulations. The vertical ticks indicate dropouts in the observed data.

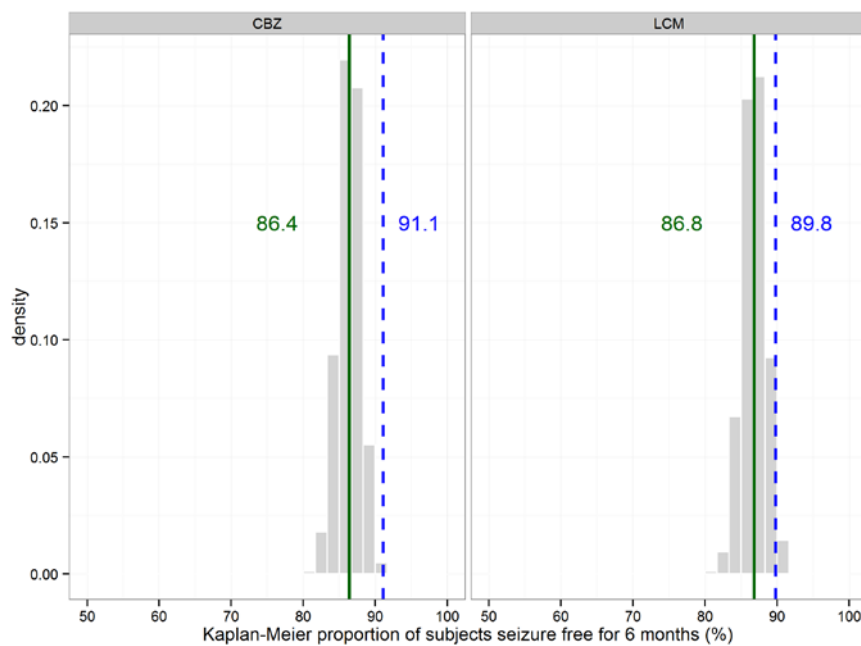


Figure 4: Posterior predictive check for the proportion of patients seizure-free for 6 months at the last evaluated dose in SP0993; patients withdrawing from the study were censored. The grey histograms show the distribution of outcomes from 500 study replicates; the solid green line shows the median of the replicates and the dotted blue line indicates the observed (i.e. Kaplan-Meier estimated) percentages in SP0993 [8].

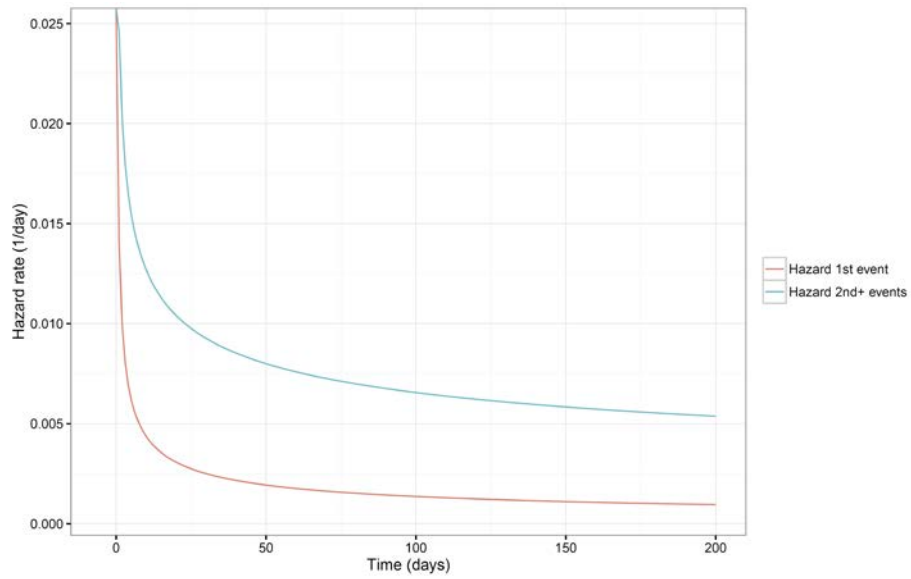


Figure 5: Simulated hazard curve at the first dose level using the typical parameter estimates as in Table 3, to illustrate a) the decrease in hazard over time and b) the higher hazard for second and more seizures compared to the first seizure.

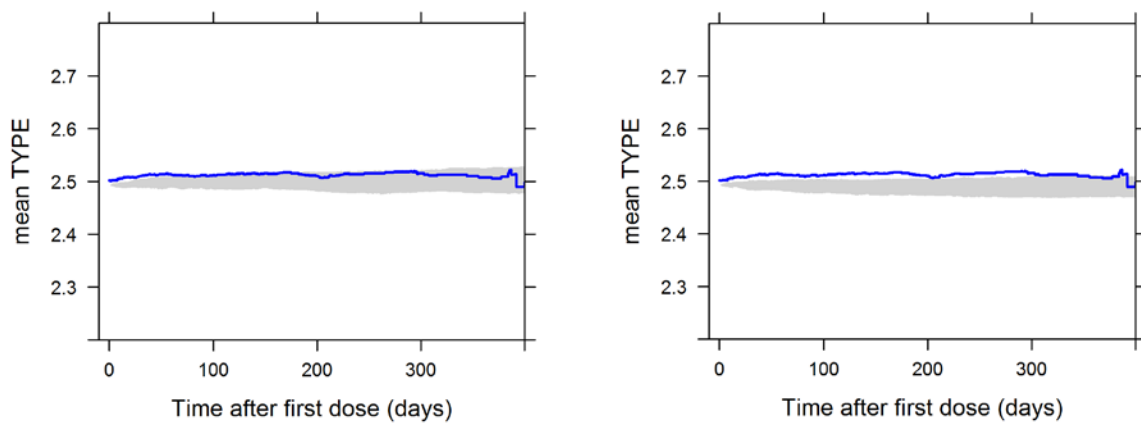


Figure 6: Kaplan-Meier covariate plot comparing two models including (left) or not (right) the effect of drug TYPE on dropout. The blue line is the 'running' mean of TYPE (3=LCM, 2=CBZ), calculated at each event time for the observations; the shaded area is the 95% prediction interval